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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/28/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/771,503	YUE ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE f this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 2, 5-7, 11 and 13 have been amended. Claims 14-21 remain withdrawn from consideration. Claims 1-13 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The rejection of claim 6 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in light of applicants amendment.

The rejection of claims 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

Claim 11 is drawn to a method for using a cDNA to detect expression of a nucleic acid in a sample comprising hybridizing the composition of claim 4 to a nucleic acid sample under conditions to form at least one hybridization complex; and detecting hybridization complex formation, wherein complex formation indicates expression of the nucleic acid in the sample, wherein the cDNA is differentially expressed when compared with a standard and diagnostic of colon cancer or colon polyps. The method is vague and indefinite in that there is no definition or limitation for "a standard"; and there is no active method step linking the outcome of comparison with said standard to the diagnosis of colon cancer or colon polyps.

Applicant argues that the meaning of the term "standard" is readily understood by one of skill in the art , and that the specific meaning of the term is set forth in the specification on page 18 which recites that "standard" values can be obtained by using values obtained from "normal subjects". This has been considered but not found persuasive. The specification is not providing a definition for a "standard value" but suggested how one can be obtained after experimentation. Therefore, the specification is not setting forth the metes and bounds of a standard value but suggesting how one can be obtained.

The rejection of claim 2, 8-10, 12 and 13 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. The rejection of claim 7 and 11 is withdrawn in light of applicants amendments.

(A)As drawn to polynucleotides comprising EST sequences

Claim 2 is drawn to an isolated DNA comprising SEQ ID NO:3-5 or the complement of SEQ ID NO:3-5. SEQ ID NO:3-5 are partial DNA sequences consisting of residues 1-276, 1-497 and 1-606 of SEQ ID NO:2. Claim 2 is drawn to a genus of nucleic acids in that it encompasses any nucleic acid sequence that minimal comprises SEQ ID NO:3- within it, including any full gene which contains the sequence, and any fusion constructs. The specification does not address whether the partial cDNA sequences cross exon/intron splice junctions which would exclude the possibility of the claims reading on a full length gene. Therefore when given the broadest reasonable interpretation the claim encompasses full length genes and cDNAs that are not fully described. It is noted that the description of a full length open reading frame is not a description of a gene as eukaryotic genes are expected to have introns and regulatory regions, such as promoters.

A description of a genus of nucleic acids may be achieved by means of recitation of representative number of cDNAs defined by nucleotide sequence falling within the scope of the genus which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lily & Co, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Here the specification discloses only SEQ ID NO:3-5 as structural features shared by members of the claimed genus. Since the claimed genus encompasses genes yet to be discovered, and DNA construct that encode fusion proteins, the structural features of SEQ ID NO:3-5 do not constitute a substantial portion of the claimed genus. Therefore, the disclosure of SEQ ID NO:3-5 does not provide an adequate description of the claimed genus. Amendment of product claims drawn to SEQ ID NO:3-5 to nucleic acids consisting of, rather then comprising, would obviate this part of the rejection.

Applicant contends that amendment of claim 2, section b, to read on "selected from a nucleic acid sequence consisting of SEQ ID NO:4 or 5" overcomes this rejection. This has been considered but not found persuasive. Claim 2(b) is drawn to an isolated cDNA comprising a fragments of SEQ ID NO:2 and thus persists in reading on cDNA, genes and chromosomes which minimally comprise the partial EST sequences of SEQ ID NO:4 and 5. Reconstruction of section b of claim 2 to be an independent claim drawn to a fragment of SEQ ID NO:2 selected from the group consisting of SEQ ID NO:4-5 would not be subject to this rejection.

(B)As drawn to a method of using a cDNA to detect expression of a nucleic acid, wherein said cDNA is not the complementary sequence to SEQ ID NO:2.

Claim 8 is drawn to a method for using a cDNA to detect expression of a nucleic acid in a sample comprising hybridizing the composition of claim 4 to nucleic acid in the sample. Claim 4 clearly encompasses both the cDNA of claim 1 and the complement of the isolated nucleic acid of claim 1. Thus, claim 8 is drawn in part to a method of using the nucleic acid encoding SEQ ID NO:1 for the detection of expression of nucleic acids within a sample. Claims 8-13 depend upon a genus of expressed nucleic acids encompassing nucleic acids which encode intelectin and nucleic acids which encode a completely unrelated protein, as nucleic acids which hybridize to SEQ ID NO:2 would translate in the reverse of SEQ ID NO:2 and therefore would not encode intelectin or be expected to encode any protein related to intelectin. The specification teaches a method of using the complementary nucleic acid to the nucleic acids which encode SEQ ID NO:1 for the detection of the nucleic acids encoding intelectin within a sample. Since the claims depend upon a protein yet to be discovered, i.e. the translated product of the sequence which hybridizes to the nucleic acids encoding SEQ ID NO:1, the disclosure of SEQ ID NO:2 is insufficient to describe the claimed genus.

Applicant argues that one of skill in the art would known how to use the claimed methods drawn to the cDNA encoding SEQ ID NO:1 or the complement thereof because it is a well known fact that most nucleic acids exist in the double-stranded form. This has been considered but not found persuasive. Firstly, applicants are incorrect in in asserting that "most nucleic acids exist in double-stranded form. For instance, most of the nucleic acids found within a cell are RNA, which is single stranded. Secondly, it is well known in the art that detection of said RNA requires the complementary polynucleotide strand, and thus, single stranded probes,

which hybridize only to the single stranded RNA. Thirdly, this is a rejection under 112, first for lacking written description, and it is not a question of whether one of skill in the art would known how to use said methods, but whether applicant has provided an example which describes the claimed species. In the case of claims 8-10 and 12-13, when given the broadest reasonable interpretation, read on the detection of the complement of SEQ ID NO:2, or the detection of the complement of the nucleic acids encoding SEQ ID NO:1 in a sample.

(C)As drawn to a method of using a cDNA to screen a plurality of molecules which specifically bind the cDNA (peptides, transcription factors).

Claim 12 is drawn to a method for using a cDNA to screen a plurality of molecules or compounds the method comprising combining the cDNA of claim 1 with a plurality of molecules under conditions to allow for specific binding, detecting the specific binding, thereby identifying a molecule of compound which specifically binds to the cDNA. Claims 13 embodies the molecules or compounds of DNA, RNA, peptide nuclei acids, artificial chromosomes, peptides or transcription factors. The claims rely on a genus of molecules and compounds which specifically bind to the cDNA of claim 1. The specification describes a method of detecting colon cancer or colon polyps wherein hybridization of a nucleic acid probe which binds to SEQ ID NO:1 is indicative of colon cancer or colon polyps. The specification does not describe any other active methods steps in which detection of a nucleic acid probe to the complement of SEQ ID NO:2 is indicative of colon cancer or colon polyps, or any other disease. One of skill in the art would conclude that applicant has not provided a representative number of species which anticipate the claimed genus, wherein the species comprise a method step for the detection of the complement of SEQ ID NO:2, nor are there a representative number of species of method steps for the detection of disease or pathological conditions beyond those of colon cancer or colon polyps. The general knowledge and skill in the art does not supplement the omission in the disclosure because specific not general guidance is what is needed. In reference to claims 12 and 13, the specification has not described any method steps wherein specific peptides or transcription factors are identified by binding to SEQ ID NO:2 or the complement of SEQ ID NO:2. It is well known in the art that DNA sequences comprising the complementary base part of a given sequence will form a hybridization with a given sequence under appropriate physical

conditions. However, in the case of generic proteins and generic transcription factors as recited in the method limitation of claim 13, the general knowledge and skill in the art do not supplement the omitted description because the there is no nexus between protein sequences which bind to DNA and transcription factor and the primary DNA sequence given by the nucleic acids which encode SEQ ID NO:1. Further the art defines a transcription factor as any of the multiple ancillary DNA-binding proteins which interact with the cis-regulatory DNA sequences to control gene expression (Reiger, Glossary of Genetics and Cytogenetics, 1991, page 481). The specification fails to disclose the cis-regulatory region of SEQ ID NO:2, which is commonly located upstream in the promoter region of the gene. The specification does not reduce to practice claim 13 and no peptides or transcription factors have been disclosed which have been isolated by the claimed method. Thus the specification does not provide adequate written description for claim 13 because disclosure of hybridization to DNA sequences does not anticipate method steps involving DNA-peptide binding or DNA-transcription factor-binding. One of skill in the art would reasonably conclude that applicant did not disclose a representative number of species representative of the claimed method with regard to method steps involving transcription factors. Claim 13 also carries the limitation of selecting "peptides" to allow for specific binding to the DNA comprising the nucleic acids encoding SEQ ID NO:1 or the complement of SEQ ID NO:1. The specification has not described any method steps wherein specific peptides were screened for binding to the cDNA of claim 1. Further, the art recognizes that there is no reliable nexus between the binding of a protein to a DNA sequence and the primary nucleotide sequence as exists for polynucleotide-polynucleotide binding. For instance, Saenger (Principles of Nucleic Acid Structure, 1984, pages 385-431) teaches that protein-nucleotide interactions depend on two main characteristic, the overall topology of the two partners and the specific interactions between individual nucleotide and protein main chain or side-chain atoms (page 408, lines 1-4) and that a wide range of protein-nucleotide interactions does exist wherein the nucleic acid interacts with the protein by means of both the amino acid side chains and the peptide functional groups (page 418, lines 8-13) . More recent publications corroborate the teachings of Saenger, such as taught by Wolfe et al (Structure, 2001, Vol. 9, pp. 717-723) who teach that the interaction between zinc finger proteins and DNA is complex and reveals differences between the interaction of individual nucleotides and amino acid side chains

and that the zinc-finger-DNA interaction cannot be determined by a "meaningful recognition code" of the nucleic acid even for zinc finger proteins which are known to bind to DNA. One of skill in the art would readily conclude that the description of a method wherein the nucleic acid of claim 1 is hybridized to a polynucleotide which hybridizes to the nucleic acid of SEQ ID NO:2 does not adequately anticipate claims 12-13 as drawn to a method of screening for proteins and transcription factors which bind to either SEQ ID NO:2 or the complement of SEQ ID NO:2.

Claims 4 and 8-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting colon cancer or colon polyps comprising the detection of SEQ ID NO:2 or the nucleic acids encoding SEQ ID NO:1 in a sample of colon tissue, and a composition comprising the complement of the nucleic acid sequence encoding SEQ ID NO:1 and a labeling moiety, does not reasonably provide enablement for a method of detecting any other disease or condition comprising the detection of SEQ ID NO:2, the complement of SEQ ID NO:2, the nucleic acid sequences encoding SEQ ID NO:1, or the complement thereof, or a composition comprising the nucleic acids encoding SEQ ID NO:1 and a labeling moiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claim 8 is drawn to a method for using a cDNA to detect expression of a nucleic acid in a sample comprising hybridizing the composition of claim 4 to nucleic acid in said sample. Claim 4 clearly encompasses both the cDNA of claim 1 and the complement of the isolated nucleic acid of claim 1. Thus, claim 8 is drawn in part to a method of using the nucleic acid encoding SEQ ID NO:1 for the detection of expression of nucleic acids within a sample. For the reasons stated above, sequence which are complementary to SEQ ID NO:2 or the nucleic acids encoding SEQ ID NO:1 would not be expected to encode intelectin or a protein similar to intelectin. It is not known how one of skill in the art would use the detection of the hybridization complex between the composition of claim 4 comprising the cDNA sequence of claim 1 and a labeling moiety and the expressed nucleic acids in a sample, as said hybridization complex would not be expected to be indicative of colon cancer or polyps. Further, the specification has not provided guidance as to other diseases or conditions beyond those of colon

cancer or colon polyps which would be indicative of the differential expression of the nucleic acids encoding SEQ ID NO:1 or the complement thereof. One of skill in the art would be subject to undue experimentation without reasonable expectation of success in order practice the broadly claimed methods.

Applicant argues that the use of both strand of the nucleic acids encoding SEQ ID NO:1 in methods of nucleic acid detection is not dependent on any protein which may or may not be encoded by the complementary strand of SEQ ID NO:2. Applicant further argues that because the double stranded nature of DNA , the presence of SEQ ID NO:2 or its complete complement is indicative of the presence of SEQ ID NO:2 itself in the sample, and therefore the use of the complementary strand is clearly enabled by the specification. This has been considered but not found persuasive. If applicant were to amend claim 8 to include the limitation of claim 9, the presence of the complementary strand of DNA would be expected, however, in the absence of this step, or a step involving the production of a cDNA from the sample the complementary strand would not be expected . Applicants attention is drawn to the findings of Atlas Power v. DuPont, 224 USPQ 409, 414 (Fed. Cir, 1984), where a significant number of inoperative embodiments was deemed to indicate an undue amount of experimentation. Secondly, claims 8-10 are not limited to the detection of colon cancer and colon polyps, and therefore, read on a sample of DNA obtained from any organ or tissue, and additionally, genomic DNA. The specification has not taught a correlation between the detection of complement of SEQ ID NO:2 in genomic DNA and any disease or condition. Any other organ or tissue which comprise an expressed DNA sequence which was the complement of SEQ ID NO:2 would be encompassed by the claims, and the specification has provided no teachings regarding these diseases or conditions or the organ or tissue types involved.

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for colon cancer or colon polyps comprising the detection of nucleic acids which bind to the complement of SEQ ID NO:2 or the complement of nucleic acids encoding SEQ ID NO:1 in a sample of colon tissue, does not reasonably provide enablement for a method of screening for any other disease or condition comprising the detection of nucleic acids which bind to the SEQ ID NO:2, the complement of

SEQ ID NO:2, the nucleic acid sequences encoding SEQ ID NO:1, or the complement thereof, or a composition comprising the nucleic acids encoding SEQ ID NO:1 and a labeling moiety., does not reasonably provide enablement for. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 12 is drawn to a method of using a cDNA to screen a plurality of molecules or compounds, the method comprising combining the cDNA of claim 1 with a plurality of molecules or compounds under conditions to allow for specific binding and detecting specific binding thereby identifying a molecule or compound which specifically binds to the cDNA. Claim 13 embodies the method of claim 12 wherein the molecules or compounds are selected from DNA molecules, RNA molecules, peptide nucleic acids, artificial chromosome constructions, peptides or transcription factors. The specification teaches only the binding of a nucleic acid sequence to the nucleic acids encoding SEQ ID NO:1 or SEQ ID NO:2, wherein detection of the hybridization complex is indicative of colon caner or colon polyps. The species of DNA molecules, RNA molecules, peptide nucleic acids and artificial chromosome constructs are commensurate in scope with the teachings of the specification, with regard to the detection of the nucleic acids encoding SEQ ID NO:1 and colon cancer or colon polyps, however, the specification provides no teachings of how to use the broadly claimed molecules which bind to the complement of the nucleic acids which encode SEQ ID NO:1 , nor how to use "peptides" and "transcription factors" which bind to a nucleic acid sequence comprising the polynucleotide of claim 1. As stated above, Reiger, (Glossary of Genetics and Cytogenetics, 1991, page 481). defines a transcription factor as any of the multiple ancillary DNA-binding proteins which interact with the cis-regulatory DNA sequences to control gene expression The specification fails to disclose the cis-regulatory region of SEQ ID NO:2, which is commonly located upstream in the promoter region of the gene. The specification has failed to teach the sequence of a c-s-regulatory DNA sequence upstream of the protein coding sequence. With regard to "peptides" the specification has failed to identify a peptide binding sequence with the claimed DNA sequence and has not taught how to make or use peptides or transcription factors . Clearly, one of skill in the art would not know how to use the multitude of potential peptides that would bind to the claimed DNA, and the specification has failed to teach a single example of such. Further,

the specification has failed to teach how to use a "transcription factor" isolated by the claimed method. It is noted in the art that although a limited number of transcription factors are correlated with cancerous cells, there is as of four years past the claimed priority date of the instant application no means of controlling specific transcription factor activity within the cells (abstract, Darnell, Nat Rev Cancer, 2002, Vol. 2, pp. 740-749). Further, section 2164.03 of the M.P.E.P. states

> A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. In re Vickers, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); In re Cook, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work

Clearly, the disclosure that the hybridization complex between the nucleic acids which encode SEQ ID NO:1 and a labeled probe, wherein the level of hybridization complex is indicative of colon cancer or coon polyps is not commensurate in scope with the claimed method of using a cDNA for screening a plurality of molecules or compounds, wherein the only criteria of the assay is the detection of binding to either the nucleic acids which encode SEQ ID NO:1 or the complement thereof. As stated by the MPEP, the disclosure of a single species usually does not provide adequate basis to support generic claims. Claim 12 is generic because the only criteria of the assay is the binding to either the nucleic acids which encodes SEQ ID NO:1 or the complement thereof , without reference to colon cancer or colon polyps. Accordingly, there is no enablement for the broadly claimed method beyond the screening of molecules which hybridize to the nucleic acids which encode SEQ ID NO:1, wherein it is determined that the nucleic acids are indicative of colon cancer or colon polyps.

The rejection of claims 1, 2, 4-10, 12 and 13 under 35 U.S.C. 102(e) as being anticipated by Pierce et al (U.S. 6,146,849) is maintained for reasons of record. Claims 1 is drawn in part to

the complement of an isolated cDNA comprising a nucleic acid sequence encoding SEQ ID NO:1. Claim 2 is drawn in part to the complement of: an isolated DNA sequence comprising SEQ ID NO:2; SEQ ID NO:3, 4 and 5. Claim 4 embodies the complement of claim 1 and a labeling moiety. Claim 5 is drawn to a vector comprising the cDNA of claim 1. Claim 6 is drawn to a host cell comprising the vector of claim 5. Claim 7 is drawn to a method of producing a protein comprising culturing the host cell of claim 6,. Claim 8 is drawn to a method for using a cDNA to detect expression of a nucleic acid comprising hybridizing the composition of claim 4 to nucleic acid in a sample and detecting the hybridization complex. Claim 9 is drawn to the method of claim 8 further comprising amplifying the nucleic acid in the sample prior to hybridization. Claim 10 embodies the method of claim 8 wherein the composition is attached to a substrate. Claim 12 is drawn to a method of using a cDNA to screen a plurality of molecules or compounds under conditions to allow specific binding, and detecting specific binding, thereby identifying a molecule or compound which specifically binds to the cDNA. Claims 13 specifically embodies the method of claim 12 wherein the molecules or compounds are selected from DNA, RNA, peptide nuclei acids, artificial chromosomes constructions, peptides or transcription factors.

The specification defines "complement" on page 7, lines 11-13, as a nucleic acid molecules which are completely complementary over their full lengths to a cDNA of the sequence listing and which will hybridize to cDNA or mRNA under conditions of high stringency. Pierce et al disclose the cDNA clone of HL-13 (SEQ ID NO:5) which encodes (nucleotides 34-1011, column 3, lines 56-61) an amino acid sequence identical to the instant SEQ ID NO:1 with the exception of an arginine residue at position 103. The complement of this CDNA would hybridize under stringent conditions to the instant SEQ ID NO:2 because there is only one nucleotide difference out of 975 nucleotides of coding region, as the substitution of a "A" for the "G" as nucleotide position 341 of the attached sequence alignment would result in the substitution of His for Arg. Furthermore, the instant SEQ ID NO:3-5 would hybridize to the complement of the coding sequence of SEQ ID NO:5 as there would be no mismatched nucleotides for SEQ ID NO:3, and only a single mismatched nucleotide for SEQ ID NO:4 and 5. Pierce et al disclose that at conditions of high stringency, molecules having about 95-100%

sequence identity form hybridization complexes (column 4, lines 14-20) which would encompass the instant SEQ ID NO:2-5 and the cDNA encoding the instant SEQ ID NO:1. Pierce et al disclose the pQE-9 QIAexpress vector comprising HL-13, and the expression of said vector in E coli to obtain the recombinant protein (column 10, lines 15-35 and column 17, lines 43-51), this fulfilling the specific embodiments of claims 5-7. Pierce et al disclose a method for detecting the expression of a HL-13 nucleic acid in a sample comprising the use of radio labeled probes. (Column 13, lines 1-19, Table 3 and column 18, lines 9-35), thus fulfilling the specific embodiments of claim 8.. Pierce et al teach detection of hybridization complexes with expressed DNA by means of Northern Blot analysis, therefore the radio labeled probes would be attached to the membrane after washing, thus fulfilling the specific embodiment of claim 10. The probes used by Pierce et al comprise complementary sequence which would hybridize under stringent conditions to the nucleic acid encoding SEQ ID NO:1. Pierce et al disclose that the expression of the HL-13 nucleic acid was detected in the human small intestine stretch lambda gt10 cDNA library (column 25, lines 23-29). The mRNA used to make the library was subjected to amplification by a reverse polymerase in the synthesis of cDNA from RNA, thus fulfilling the limitation of claim 9 drawn to amplification of the nucleic acids prior to hybridization. Further, Pierce et al disclose that somatic cell hybrid DNAs were screened by PCR prior to FISH analysis, again fulfilling the specific embodiment of claims 8 and 9 (column 27, lines 16-50). Pierce et al disclose primers used to make genomic clones comprising nucleic acids which would hybridize under stringent conditions to the nucleic acid which encode SEQ ID NO:1, thus fulfilling the specific embodiment of claims 12 and claim 13, drawn to artificial chromosome constructs.

Pierce et al disclose a method of using a cDNA to screen a plurality of molecules or compounds comprising the hybridization of radio labeled probes that would hybridize under stringent conditions to the nucleic acid sequence encoding SEQ ID NO:1 to the lambda stretch gt10 cDNA library (column 25, lines 23-29), and in Northern blots with various tissues (column 18, lines 9-35), thus fulfilling the limitations of claims 12 and 13, drawn to DNA molecules and RNA molecules.

Applicant argues that the definition of complement given in the specification as a nucleic acid molecule which is completely complementary over its full length to a cDNA of the

sequence listing requires that the complementary polynucleotide be of the same length as SEQ ID NO:1 or the nucleic acids encoding SEQ ID NO:2. this has been considered but not found persuasive. The definition states that the nucleic acid which is the complement must be completely complementary over its full length, it is noted that this limitation is set out in reference to the "nucleic acid" and not to the "cDNA". Thus the claims read on isolated DNAs comprising nucleic acids which are completely complementary in that said nucleic acids contain no misparings with the cDNA of SEQ ID NO:2 or the nucleic acid encoding SEQ ID NO:1. The definition in the specification does not exclude complementary nucleic acids which are shorter than SEQ ID NO:2. Further the claims read on cDNA comprising said nucleic acids having this property and therefore do not require that the entire cDNA be completely complementary to SEQ ID NO:2 of the nucleic acids encoding SEQ ID NO:1.

The rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by The New England Biolabs Catalog (1993-1994, page 91) is maintained for reasons of record. The New England Biolabs Catalog discloses random hexamers which will be complementary across their full length to the nucleic acids encoding SEQ ID NO:1 and SEQ ID NO:2-5. Applicant argues that the random hexamers are not prior art as the specification defines "complement" on page 7 as a nucleic acid which is completely complementary over its full length and will hybridize to the cDNA or mRNA under conditions of high stringency. This has been considered but not found persuasive. The limitation that the nucleic acid of the complement must be completely complementary over their full length is in reference to the nucleic acid of the complement, not to the nucleic acid of the sense strand. The definition recited therein on page 7 does not exclude smaller fragments of the disclosed SEQ ID NO:1 which are completely complementary to SEQ ID NO:1 across their full lengths. The random hexamers would be completely complementary across their full lengths to SEQ ID NO:1.

All other rejections and objections as set forth in Paper No. 15 are withdrawn.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
8/25/03